PHTHALATE EXPOSURE AND BREAST-CANCER RISK ACCORDING TO *PPARγ* AND *PPARGC1B* GENOTYPES

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Background and Aims: Some phthalic acid diesters (phthalates) have recently been associated with breast cancer (BC). In this study we evaluated if that association is modified according to *PPARγ* and *PPARGC1B* genotypes.
Methods: 208 BC cases were age-matched with 220 population controls from the north of Mexico. Urine concentrations of nine phthalate metabolites were determined by isotope dilution/high-performance liquid chromatography and mass spectrometry. Genotyping of variant *Pro12Ala* (rs1801281) of the *PPARγ* gene and variants *Ala203Pro* (rs7732671) and *Val279Ile* (rs17572019) of the *PPARGC1B* gene were carried out by traditional PCR with TaqMan probes.
Results: The three polymorphisms under study were in Hardy-Weinberg equilibrium, with a minor allele frequency of 0.11*,* 0.14, and 0.14 for the *Pro12Ala*, *Ala203Pro*, and *Val279Ile* variants respectively. Only the association between the higher levels of urinary mono-(2-ethylhexyl) phthalate (MEHP) concentration with BC was modified after the stratification by the *PPARγ* gene *Pro12Ala* polymorphism alleles (for G carriers: OR=0.59 CI95%=0.25-1.39; for C carriers: OR=1.50 CI95%=1.08-2.08); and the association between the mono-iso-butyl phthalate (MiBP) with BC in women with higher urinary concentrations was modified after the stratification by the *PPARGC1B* gene *Ala203Pro* polymorphism alleles (for C carriers OR=1.12 CI95%=0.55-2.27; for G carriers OR=0.67 CI95%=0.44-1.01).
Conclusions: Our results suggest the presence of a gene-environment interaction influencing BC risk that could be determined by the magnitude of exposure.
Keywords: breast cancer, phthalates, urinary metabolites, PPARγ*, PPARGC1B*, gene-environment interaction.